Identification and prospective isolation of a mesothelial precursor lineage giving rise to smooth muscle cells and fibroblasts for mammalian internal organs, and their vasculature.

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Public Summary:
Fibroblasts and smooth muscle cells are the main cell types that produce and remodel the connective tissue–the substances that support, connect, and separate different types of tissues and organs in the body. Although these cell types are important in embryonic development and the normal functioning of organs, their origins in the embryo are not completely defined. Here, we show that the mesothelium can develop these two cell types. The mesothelium is a layer of tissue that covers all the internal organs on their outer surfaces. We have shown by live imaging and transplantation experiments that mesothelium generates fibroblasts and smooth muscle cells. We identified mesothelin as a protein on the mesothelium. Using a chemical that specifically binds to mesothelin, we were able to separate mesothelial cells from larger populations of mixed cells and demonstrate they could generate, in a culture dish, fibroblasts and smooth muscle cells. These mesothelin-expressing cells, when tracked with a label in the mouse embryo, gave rise to fibroblasts, all smooth muscle cells, and blood vessels within the internal organs. The isolation of these precursors of fibroblasts and smooth muscle cells may allow for their use in regenerative medicine and expands our ability to study and understand these precursors and their progeny.

Scientific Abstract:
Fibroblasts and smooth muscle cells (FSMCs) are principal cell types of connective and adventitial tissues that participate in the development, physiology and pathology of internal organs, with incompletely defined cellular origins. Here, we identify and prospectively isolate from the mesothelium a mouse cell lineage that is committed to FSMCs. The mesothelium is an epithelial monolayer covering the vertebrate thoracic and abdominal cavities and internal organs. Time-lapse imaging and transplantation experiments reveal robust generation of FSMCs from the mesothelium. By targeting mesothelin (MSLN), a surface marker expressed on mesothelial cells, we identify and isolate precursors capable of clonally generating FSMCs. Using a genetic lineage tracing approach, we show that embryonic and adult mesothelium represents a common lineage to trunk FSMCs, and trunk vasculature, with minimal contributions from neural crest, or circulating cells. The isolation of FSMC precursors enables the examination of multiple aspects of smooth muscle and fibroblast biology as well as the prospective isolation of these precursors for potential regenerative medicine purposes.